

## Complete Summary

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### GUIDELINE TITLE

Use of strontium<sup>89</sup> in patients with endocrine-refractory carcinoma of the prostate metastatic to bone.

### BIBLIOGRAPHIC SOURCE(S)

Cancer Care Ontario Practice Guideline Initiative (CCOPGI). Use of strontium<sup>89</sup> in patients with endocrine-refractory carcinoma of the prostate metastatic to bone [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2001 Oct [online update]. Various p. (Practice guideline report; no. 3-6). [14 references]

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## SCOPE

### DISEASE/CONDITION(S)

Carcinoma of the prostate

### GUIDELINE CATEGORY

Treatment

### CLINICAL SPECIALTY

Internal Medicine  
 Oncology  
 Radiation Oncology  
 Urology

### INTENDED USERS

Physicians

## GUIDELINE OBJECTIVE(S)

To determine the indications for the routine use of strontium<sup>89</sup> in patients with metastatic prostate cancer

## TARGET POPULATION

Adult patients with stage D endocrine/hormone-refractory prostate cancer in two different clinical situations:

- Patients with multiple sites of painful bony metastases
- Patients receiving local radiotherapy for isolated painful bony metastases

## INTERVENTIONS AND PRACTICES CONSIDERED

1. Treatment with strontium<sup>89</sup>
2. Alternative management strategies, including step-wise use of analgesic therapy, involved-field radiotherapy, wide-field radiotherapy, and other supportive palliative measures

## MAJOR OUTCOMES CONSIDERED

- Markers of effective palliation (e.g., change in analgesic requirements, functional status, quality of life evaluation)
- Time to further radiotherapy
- Patient survival
- Treatment toxicity

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)  
Hand-searches of Published Literature (Secondary Sources)  
Searches of Electronic Databases  
Searches of Unpublished Data

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

#### 1997 Guideline

MEDLINE and CANCERLIT searches were done for the years 1985-April 1997. The search terms included "prostatic neoplasms", "strontium89", "metastron", "89sr:", "89stron:", and "sr89". Selected bibliographies were reviewed to identify papers not included in the computerized databases. The PDQ database was searched to identify active registered trials in stage D prostate cancer.

#### 2001 Update

The original literature search was updated using MEDLINE (through September 2001), CANCERLIT (through August 2001) and the Cochrane Library (Issue 3, 2001).

#### Inclusion Criteria

Articles were selected for inclusion in this systematic review of the evidence if they were randomized controlled trials which used strontium<sup>89</sup> for stage D endocrine-refractory prostate cancer metastatic to bone. Outcomes of interest included markers of successful palliation (e.g., change in analgesic requirements, functional status, quality of life evaluation), time to further radiotherapy, patient survival and treatment toxicity.

#### NUMBER OF SOURCE DOCUMENTS

1997 Guideline

4 source documents

2001 Update

No additional evidence on this topic at that time

#### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

#### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

#### METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

#### DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

#### METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

#### DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

November 1997 Guideline

The structured review of the literature was reviewed by a subcommittee of the Genitourinary Cancer Disease Site Group (DSG). The conclusions of the subcommittee were then discussed with the entire DSG and reviewed by the Chair of the Cancer Care Ontario Practice Guideline Initiative (CCOPGI) Methods Resource Group. Comments were incorporated into the final draft by consensus.

The group reached a unanimous consensus, based on the available literature, on the role of strontium<sup>89</sup> therapy in patients with multiple painful sites of disease

who meet the listed indications for treatment (Part 1 of the original guideline document).

The group reached a majority consensus, based on the available literature, on the role of adjunctive strontium<sup>89</sup> therapy in patients receiving local radiotherapy for isolated painful metastases. The DSG concluded that the demonstrated benefits of adjunctive strontium<sup>89</sup> (with respect to analgesic intake requirements and the need for future treatments) were of uncertain clinical significance in the absence of valid quality of life data and in the absence of demonstrated benefit in patient survival. The group recommended further comparative study of adjunctive strontium<sup>89</sup> with adjunctive wide-field radiation including appropriate symptom control, quality of life, and economic evaluations (Part 2 of the original guideline document).

#### 2001 Update

The information above remains current.

#### RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

#### COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

#### METHOD OF GUIDELINE VALIDATION

External Peer Review  
Internal Peer Review

#### DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

External review by practitioners was obtained through a mailed survey consisting of nine questions asking for comments on the quality of the draft recommendations, and whether the draft recommendations should serve as a practice guideline. Written comments were invited. Follow-up reminders were sent at two weeks (postcard) and four weeks (complete package mailed again). Results were reviewed by the Genitourinary Cancer Disease Site Group.

The Coordinating Committee of the Cancer Care Ontario Practice Guidelines Initiative externally evaluated the practice guideline for final approval.

The original practice guideline was also reviewed by two external reviewers prior to publication in the journal Cancer Prevention and Control.

### RECOMMENDATIONS

#### MAJOR RECOMMENDATIONS

The evidence-based recommendations for the 2 clinical situations are as follows:

#### Part 1: Strontium<sup>89</sup> Treatment for Hormone Refractory Prostate Cancer Skeletal Metastases: Multiple Painful Sites of Disease

- Strontium<sup>89</sup> is recommended for use in patients with endocrine-refractory carcinoma of the prostate who have multiple uncontrolled painful sites of metastases on both sides of the diaphragm, not adequately controlled with conventional analgesic therapy and in whom the use of multiple single fields of external beam radiation is not possible.
- Strontium<sup>89</sup> has proven efficacy in the palliation of hormone-refractory painful bony metastases from prostate cancer.
- Strontium<sup>89</sup> has not been shown to lengthen the average duration of patient survival. There is limited evidence to determine its relative efficacy compared to wide-field irradiation. Specific indications, recommendations for administration, and the need for further data about the treatment are summarized in the original guideline document.

Indications for strontium<sup>89</sup> therapy in this clinical setting

All of the following are required:

- Established diagnosis of prostate cancer metastatic to bone
- Metastatic disease refractory to hormone therapy
- Progressive sites of pain poorly controlled with conventional narcotics
- Painful sites of disease on both sides of the diaphragm (otherwise, hemibody radiation is equally efficacious)
- Patient or tumour factors (number of involved sites, location of involved sites, or level of pain control) are relative contraindications to the use of multiple single fields of radiation as an alternative
- No evidence of impending spinal cord compression
- Adequate bone marrow reserve
- Painful bony lesions concentrate radionuclide on diagnostic scan

#### Part 2: Strontium<sup>89</sup> Treatment for Hormone-Refractory Prostate Cancer Skeletal Metastases: Adjunctive Strontium<sup>89</sup> for Patients Receiving Local Radiotherapy

- Strontium<sup>89</sup> is not recommended for routine use as an adjunct to local radiotherapy in this clinical setting.
- Strontium<sup>89</sup> is known to temporarily reduce analgesic intake and to modestly delay the need for treatment of sites of new pain, when used as an adjunct to local field radiotherapy and when compared to placebo adjunct therapy. The clinical significance of these benefits is not certain.
- Strontium<sup>89</sup> has not been shown to lengthen the average duration of patient survival in this setting and there is no evidence to determine its relative efficacy compared to wide-field irradiation. The need for further data about the treatment is summarized in the original guideline document.

CLINICAL ALGORITHM(S)

None provided

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Four randomized trials were identified from 40 articles and ten abstracts found by the literature search. Two trials compared strontium<sup>89</sup> with placebo, one compared strontium<sup>89</sup> with conventional radiotherapy (either hemibody or local field irradiation as determined prior to randomization), and the fourth trial evaluated strontium<sup>89</sup> as an adjunctive therapy with involved field radiotherapy.

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

#### Part 1. Strontium<sup>89</sup> Treatment for Hormone-Refractory Prostate Cancer Skeletal Metastases: Multiple Painful Sites of Disease

Three randomized controlled trials were available for evaluation. One randomized study compared the use of strontium<sup>89</sup> to conventional radiation (either hemibody or local field irradiation as determined prior to randomization), and the other two compared strontium<sup>89</sup> to placebo.

One of two studies comparing strontium<sup>89</sup> to placebo demonstrated the palliative efficacy of the intervention ( $p < 0.01$ ), while the other showed no benefit. A third study comparing the efficacy of strontium<sup>89</sup> with conventional radiation concluded that all treatments provided equally effective pain relief, and that improvement was sustained for at least three months in similar proportions of patients. The median duration of patient survival was neither clinically nor statistically different between groups in this study.

#### Part 2. Strontium<sup>89</sup> Treatment for Hormone-Refractory Prostate Cancer Skeletal Metastases: Adjunctive Strontium<sup>89</sup> for Patients Receiving Local Radiotherapy for Isolated Painful Metastases

One randomized controlled trial was available for evaluation. This study compared the use of strontium<sup>89</sup> to placebo injection as adjunctive treatment of patients receiving local radiotherapy for bony metastases from prostate cancer.

The randomized trial demonstrated that patients receiving strontium<sup>89</sup> had fewer analgesic requirements, fewer sites of new pain, and less need for additional local-field radiotherapy than patients receiving placebo. All of these differences were statistically significant. Differences in relief of pain at the index site and the duration of survival were neither statistically nor clinically significant.

The randomized trial demonstrated that patients receiving strontium<sup>89</sup> in addition to involved field radiation had fewer analgesic requirements, fewer sites of new pain, and less need for additional local-field radiotherapy than patients receiving placebo and involved field radiation. All of these differences were statistically

significant. Differences in relief of pain at the index site and the duration of survival were neither statistically nor clinically significant.

## POTENTIAL HARMS

The use of strontium<sup>89</sup> may cause bone marrow suppression, but clinically significant sequelae are uncommon. The use of strontium<sup>89</sup> may preclude further systemic chemotherapy and/or eligibility for clinical trials of systemic therapy. Symptoms other than those of bone marrow suppression are rare.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

- The practice guideline is not structured to be an exhaustive review of the literature relating to strontium<sup>89</sup> therapy; however, such reviews are available. Rather, the report focuses on the literature relating to the therapeutic indications for strontium<sup>89</sup> in patients with metastatic prostate cancer.
- The primary intent of this guideline is to address the effectiveness of strontium<sup>89</sup> in specific clinical circumstances. The guideline does not attempt to address the efficacy of nor provide a review of the data of alternative management strategies for men with endocrine-refractory prostate cancer.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

End of Life Care  
Living with Illness

### IOM DOMAIN

Effectiveness  
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Cancer Care Ontario Practice Guideline Initiative (CCOPGI). Use of strontium<sup>89</sup> in patients with endocrine-refractory carcinoma of the prostate metastatic to bone

[full report]. Toronto (ON): Cancer Care Ontario (CCO); 2001 Oct [online update]. Various p. (Practice guideline report; no. 3-6). [14 references]

#### ADAPTATION

Not applicable: The guideline was not adapted from another source.

#### DATE RELEASED

1997 Nov 23 (updated online 2001 Oct)

#### GUIDELINE DEVELOPER(S)

Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]

#### GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

#### SOURCE(S) OF FUNDING

Cancer Care Ontario, Ontario Ministry of Health and Long-Term Care

#### GUIDELINE COMMITTEE

Provincial Genitourinary Cancer Disease Site Group

#### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Members of the Provincial Genitourinary Cancer Disease Site Group: Dr. H. Lukka, (Chair), Radiation Oncologist; Dr. J. Barkin, Urologist; Dr. G. Bauman, Radiation Oncologist; Dr. J. Bowen, Radiation Oncologist; Dr. M. Brundage, Radiation Oncologist; Dr. J. Chin, Urologist; Dr. R. Choo, Radiation Oncologist; Dr. J. Crook, Radiation Oncologist; Dr. L. Eapen, Radiation Oncologist; Dr. N. Fleshner, Urologist; Dr. L. Klotz, Urologist; \*Dr. W. Love, Urologist; Dr. W. Orován, Urologist; \*Dr. H. Prichard, Radiation Oncologist; \*Dr. L. Reyno, Medical Oncologist; Dr. R. Segal, Medical Oncologist; Dr. T. Short, Urologist; Dr. J. Srigley, Medical Oncologist; Dr. J. Trachtenberg, Urologist; Dr. P. Warde, Radiation Oncologist; Dr. E. Winquist, Medical Oncologist; two community representatives

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\*Members that have completed term with the Genitourinary Cancer Disease Site Group.

## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Genitourinary Cancer Disease Site Group disclosed potential conflict of interest information.

## GUIDELINE STATUS

This is the current release of the guideline.

The guideline developer instituted a new format for their guidelines and evidence summaries: A SUMMARY of the original Practice Guideline or Evidence Summary, integrated with the most current information, replaces the ABSTRACT, RECOMMENDATION, BRIEF REPORT and EVIDENCE UPDATE.

The FULL REPORT, initially the full original Guideline or Evidence Summary, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the [Cancer Care Ontario Web site](#) for details on any new evidence that has emerged and implications to the guidelines.

## GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Cancer Care Ontario Web site](#).

## AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Use of strontium<sup>89</sup> in patients with endocrine-refractory carcinoma of the prostate metastatic to bone. Summary. Toronto (ON): Cancer Care Ontario (CCO), 1997 Nov 23 (updated online 2001 Oct).

Electronic copies: Available in Portable Document Format (PDF) from the [Cancer Care Ontario Web site](#).

## PATIENT RESOURCES

None available

## NGC STATUS

This summary was completed by ECRI on January 5, 1999. The information was verified by the guideline developer as of February 22, 1999. This NGC summary was updated by ECRI on December 17, 2001. The updated information was reviewed by the guideline developer as of January 10, 2002.

## COPYRIGHT STATEMENT

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